AMENDMENTS TO THE CLAIMS - Marked Up Version

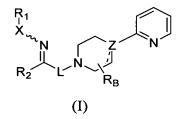
Claims 1-40, 42-63 and 65-96 are pending in the application. Claims 1-11, 18-20, 32-38, 40-48, 53, 54 and 63-69 have been elected for prosecution. Claims 12-17, 21-31, 39, 49-52, 55-62 and 70-96 have been withdrawn as being drawn to non-elected inventions. Claims 1, 3-11, 18, 19, and 20 have been amended. Claims 2, 40-48, 53, 54, and 63-69 have been cancelled.

The following list of claims will replace prior versions and listing of claims in the application:

1. (Currently Amended)

A compound of formula (I)

$$\frac{\overset{\mathsf{R}_1}{\overset{\mathsf{N}}{\mathsf{N}}}_{\mathsf{N}_{\mathsf{N}_{\mathsf{N}}}}}{\overset{\mathsf{N}}{\overset{\mathsf{N}}{\mathsf{N}_{\mathsf{N}}}}}$$



or a pharmaceutically acceptable salt thereof, wherein

X is selected from the group consisting of O and NR_A;

R_A is selected from the group consisting of hydrogen and alkyl;

R₁ is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R₂ is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl; wherein the heteroaryl and the heteroaryl moiety of the heteroarylalkyl are monocyclic, five or six membered rings containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S;

R₄ is heteroaryl wherein the heteroaryl is a monocyclic, five or six membered ring containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S;

L is C_1 - C_2 alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl;

R_B is alkyl; hydrogen or alkyl;

Z is N; and

--- is absent

2. (Cancelled) The compound according to claim 1 wherein R₃ is

3. (Currently Amended) The compound according to claim 1 wherein

X is O; and

R₂ is aryl;

and

R₄ is heteroaryl.

4. (Currently Amended) The compound according to claim 43 wherein

X is O;

 R_2 is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen.;

and

 R_4 is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin 2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

5. (Currently Amended) The compound according to claim 41 selected from the group consisting of

(1E)-1-(3-chlorophenyl)-3-(4-pyridin-2-yl-piperazin-1-yl)propan-1-one Omethyloxime;

- (1Z)-1-(3-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1E)-1-(4-chlorophenyl)-3-(4-pyridin-2-yl-piperazin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1E)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone Omethyloxime;
- (1Z)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone Omethyloxime;
- (1E)-1-(4-chlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone Omethyloxime;
- (1Z)-1-(4-chlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone Omethyloxime;
- (1E)-1-(3,4-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(3,4-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1E)-1-(3-chloro-4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;
- (1Z)-1-(3-chloro-4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;
- (1E)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1E)-1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;

- (1E)-1-(3,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone Omethyloxime;
- (1Z)-1-(3,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone Omethyloxime;
- (1E)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Oethyloxime;
- (1Z)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Oethyloxime;
- (1E)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
 - 3-[(1E)-N-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propanimidoyl]benzonitrile
 - 3-[(1Z)-N-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propanimidoyl]benzonitrile
- (1E)-1-(2,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone Omethyloxime;
- (1Z)-1-(2,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone Omethyloxime;
 - (1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;
 - (1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;
- (1Z)-1-phenyl-3 (4-pyrimidin 2-ylpiperazin-1-yl)propan-1-one oxime;
 - 1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;
 - (1E)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;
 - (1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;
 - (1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;
 - (1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;
 - (1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;
 - (1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-propyloxime;
 - (1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-propyloxime;
 - (1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-allyloxime;
 - (1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-allyloxime;

- (1E)-1-(3,5-difluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(3,5-difluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
 - ({[1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propylidene]amino}oxy)acetonitrile; 1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-butyloxime;
 - (1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-isopropyloxime;
- (1E)-1-(3,5-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(3,5-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1E)-1-(4-chloro-3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;
- (1Z)-1-(4-chloro-3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;
 - (1E)-1-(2-naphthyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;
 - (1Z)-1-(2-naphthyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;
- (1E)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Oethyloxime;
- (1Z)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Oethyloxime;
- 1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-(2,2,2-trifluoroethyl)oxime;
- 1-(4-chlorophenyl)-3-(methoxyamino)-2-[(4-pyridin-2-ylpiperazin-1-yl)methyl]propan-1-one O-methyloxime;
- 1-(4-chlorophenyl)-3-isopropoxy-2-[(4-pyridin-2-ylpiperazin-1-yl)methyl]propan-1-one-O-methyloxime;
- —— 1-(4-chlorophenyl) 2-methyl-3 (4-pyridin-2-ylpiperazin-1-yl)propan 1-one O-methyloxime;
- (1E)-1-(3,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;

- (1Z)-1-(3,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1E)-1-(2-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(2-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1E)-1-(2,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(2,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1E)-1-(4-bromophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(4-bromophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1E)-1-(3-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(3-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime;
- (1E) 1 (4 fluorophenyl) 2 (4 pyrimidin 2 ylpiperazin 1 yl)ethanone oxime;
 - (1E)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone oxime;
 - (1Z)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone oxime;
 - 2-{4-[(3E)-3-(hydroxyimino)-3-phenylpropyl]piperazin-1-yl}nicotinonitrile;
- 2-{4-[(3Z) 3-(hydroxyimino)-3-phenylpropyl]piperazin-1-yl}nicotinonitrile;
- 3-[4 (3 methylpyridin-2-yl)piperazin-1-yl]-1-phenylpropan-1-one O-ethyloxime;
- 2-{4-[3-(ethoxyimino)-3-phenylpropyl]piperazin-1-yl}nicotinonitrile;
- 2 {4-[3-(ethoxyimino)-3-(3-methylphenyl)propyl]piperazin-1-yl}nicotinonitrile;
- (1E)-1-(4-fluorophenyl)-2-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-yl]ethanone O-methyloxime;
- (1Z)-1-(4-fluorophenyl)-2-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-yl]ethanone O-methyloxime;

(1E)-1-(4-chlorophenyl)-3-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-yl]propan-1one O-methyloxime; (1Z)-1-(4-chlorophenyl)-3-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-yl]propan-1one O-methyloxime; 1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-(2hydroxyethyl)oxime; (1E)-1-(4-chlorophenyl)-3-[4-(5-hydroxypyridin-2-yl)piperazin-1-yl]propan-1one O-methyloxime; (1Z) 1 (4-chlorophenyl) 3 [4 (5-hydroxypyridin 2-yl)piperazin 1-yl]propan 1 one O-methyloxime: 1-(4-fluorophenyl) 2-[4-(5-hydroxypyridin-2-yl)piperazin-1-yl]ethanone Omethyloxime; (1E)-1-(4-chlorophenyl)-2-hydroxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime; (1Z)-1-(4-chlorophenyl)-2-hydroxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime; (1E) 1 (4-chlorophenyl) 3 (4-pyrimidin 2-ylpiperazin 1-yl)propan 1-one Omethyloxime; (1Z) 1 (4 chlorophenyl) 3 (4 pyrimidin 2 ylpiperazin 1 yl)propan 1 one O methyloxime; (1E)-1-(4-chlorophenyl)-2-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime; and (1Z)-1-(4-chlorophenyl)-2-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime. 6. (Currently Amended) The compound according to claim 1 wherein X is O; and R₂ is arylalkyl.; and R₄ is heteroaryl.

7. (Currently Amended) The compound according to claim 1-6 wherein X is O;

R₂ is arylalkyl wherein the arylalkyl is benzyl.;

and

R₄ is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin 2-yl, 3 cyanopyridin 2-yl, 5 hydroxypyridin 2-yl, 3 methylpyridin 2-yl, pyridin 2-yl, 2-pyridinium N-oxide, pyrimidin 2-yl, and thiazol-2-yl.

- 8. (Original) The compound according to claim 7 selected from the group consisting of (2E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)acetone O-methyloxime; and (2Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)acetone O-methyloxime.
- 10. (Currently Amended) The compound according to claim 1--9 wherein X is O;

 R₂ is heteroaryl wherein the heteroaryl is-pyridin-3-yl.;

 and

- 11. (Currently Amended) The compound according to claim 41 selected from the group consisting of
- (1E)-1-pyridin-3-yl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime; and

(1Z)-1-pyridin-3-yl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one Omethyloxime.

12. (Withdrawn) The compound according to claim 2 wherein

X is O;

R₂ is aryl;

Z is C;

--- is a single bond; and

 R_4 is heteroaryl.

13. (Withdrawn) The compound according to claim 2 wherein

X is O;

 R_2 is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

Z is C;

--- is a single bond; and

R₄ is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

14. (Withdrawn) The compound according to claim 13 selected from the group consisting of

1-(4-fluorophenyl)-3-[4-(1,3-thiazol-2-yl)-3,6-dihydropyridin-1(2H)-yl]propan-1-one O-methyloxime;

(1E)-1-(4-chlorophenyl)-2-[4-(1,3-thiazol-2-yl)-3,6-dihydropyridin-1(2H)-yl]ethanone O-methyloxime;

(1Z)-1-(4-chlorophenyl)-2-[4-(1,3-thiazol-2-yl)-3,6-dihydropyridin-1(2H)-yl]ethanone O-methyloxime;

(1E)-1-(4-chlorophenyl)-3-(3-methyl-3',6'-dihydro-2,4'-bipyridin-1'(2'H)-yl)propan-1-one O-methyloxime; and

(1Z)-1-(4-chlorophenyl)-3-(3-methyl-3',6'-dihydro-2,4'-bipyridin-1'(2'H)-yl)propan-1-one O-methyloxime.

15. (Withdrawn) The compound according to claim 2 wherein

X is O;

R₂ is aryl;

Z is CH;

--- is absent; and

R₄ is heteroaryl.

16. (Withdrawn) The compound according to claim 2 wherein

X is O;

R₂ is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

Z is CH;

--- is absent; and

- 17. (Withdrawn) The compound according to claim 16 selected from the group consisting of
- (1E)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperidin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperidin-1-yl)propan-1-one Omethyloxime;
- 2-{1-[(3E)-3-(4-chlorophenyl)-3-(methoxyimino)propyl]piperidin-4-yl}pyridinium N-oxide;
- 2-{1-[(3Z)-3-(4-chlorophenyl)-3-(methoxyimino)propyl]piperidin-4-yl}pyridinium N-oxide;

 $2-\{1-[(2E)-2-(4-fluorophenyl)-2-(methoxyimino)ethyl] piperidin-4-yl\} pyridinium N-oxide; and$

 $2-\{1-[(2Z)-2-(4-fluorophenyl)-2-(methoxyimino)ethyl] piperidin-4-yl\} pyridinium N-oxide. \\$

18. (Currently Amended) The compound according to claim 1 wherein

X is NR_A; andkl

R₂ is aryl;.

and

----R₄ is heteroaryl.

19. (Currently Amended) The compound according to claim 1–18wherein X is NR_A;

R₂ is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen.;

and

R₄ is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N oxide, pyrimidin-2-yl, and thiazol-2-yl.

- 20. (Currently Amended) The compound according to claim 19 that is 1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone methylhydrazone.
- 21. (Withdrawn) The compound according to claim 2 wherein

X is NR_A ;

R₂ is aryl;

Z is CH;

--- is absent; and

R₄ is heteroaryl.

22. (Withdrawn) The compound according to claim 2 wherein X is NR_A;

R₂ is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

Z is CH;

--- is absent; and

R₄ is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

23. (Withdrawn) The compound according to claim 22 that is 1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperidin-1-yl)ethanone methylhydrazone.

24. (Withdrawn) The compound according to claim 1 wherein R_3 is

25. (Withdrawn) The compound according to claim 24 wherein R_2 is aryl; and R_4 is heteroaryl.

26. (Withdrawn) The compound according to claim 24 wherein

R₂ is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

27. (Withdrawn) The compound according to claim 26 selected from the group consisting of

1-(4-fluorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one Omethyloxime;

1-(4-fluorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one Oethyloxime;

1-(4-fluorophenyl)-3-(3-pyridin-2-ylpiperidin-1-yl)propan-1-one O-methyloxime;

1-(4-chlorophenyl)-3-(3-pyridin-2-ylpiperidin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-chlorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one Omethyloxime;

(1Z)-1-(4-chlorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one Omethyloxime;

2-{1-[2-(4-fluorophenyl)-2-(methoxyimino)ethyl]piperidin-3-ylpyridinium Noxide; and

2-{1-[3-(4-fluorophenyl)-3-(methoxyimino)propyl]piperidin-3-yl}pyridinium Noxide.

28. (Withdrawn) The compound according to claim 1 wherein R₃ is

29. (Withdrawn) The compound according to claim 28 wherein

R₂ is aryl; and

R₄ is heteroaryl.

30. (Withdrawn) The compound according to claim 28 wherein

 R_2 is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

- 31. (Withdrawn) The compound according to claim 30 selected from the group consisting of
- (1E)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one Omethyloxime;
- (1Z)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one Omethyloxime;
- (1E)-1-(4-fluorophenyl)-2-(3-pyrazin-2-ylpyrrolidin-1-yl)ethanone Omethyloxime;
- (1Z)-1-(4-fluorophenyl)-2-(3-pyrazin-2-ylpyrrolidin-1-yl)ethanone Omethyloxime;
 - (1E)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one oxime;
 - (1Z)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one oxime; and
 - (1Z)-1-(4-fluorophenyl)-2-(3-pyrazin-2-ylpyrrolidin-1-yl)ethanone oxime.
- 32. (Previously Amended) A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (I) according to claim 1 in combination with a pharmaceutically acceptable carrier.
- 33. (Previously Amended) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof in combination with a pharmaceutically acceptable carrier.
- 34. (Previously Amended) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a

compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof in combination with a phosphodiesterase 5 inhibitor.

- 35. (Previously Amended) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof in combination with an adrenergic receptor antagonist.
- 36. (Previously Amended) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof in combination with a dopamine agonist.
- 37. (Previously Amended) A method of treating male erectile dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof.
- 38. (Previously Amended) A method of treating female sexual dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof.
- 39. (Withdrawn) A method of treating cardiovascular disorders, inflammatory disorders, attention deficit hyperactivity disorder, Alzheimer's disease, drug abuse, Parkinson's disease, schizophrenia, anxiety, mood disorders or depression in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or prodrug thereof.

40. (Cancelled) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (Ia)

$$R_1$$
 X
 N
 R_2
 L
 R_3
 R_3

or a pharmaceutically acceptable salt-or-prodrug-thereof, wherein

X is selected from the group consisting of O and NR_A;

R_A is selected from the group consisting of hydrogen and alkyl;

R₁ is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R₂ is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl; wherein the heteroaryl and the heteroaryl moiety of the heteroarylalkyl are mocyclic, five or six membered rings containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S;

R₃ is

R₄ is heteroaryl; wherein the heteroaryl is a monocyclic, five or six membered ring containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S;

L is alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl;

R_B is alkyl;

Z is N; and

--- is absent or a pharmaceutically acceptable salt or prodrug thereof in combination with a pharmaceutically acceptable carrier.

41. (Cancelled) The method according to claim 40 wherein R₃ is

42. (Cancelled) The method according to claim 40 wherein

X is O;

R₂ is aryl;

and

R₄ is heteroaryl.

43. (Cancelled) The method according to claim 40 wherein

X is O;

R₂ is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

and

R₄ is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

44. (Cancelled) The method according to claim 43 where the compound of formula (Ia) is selected from the group consisting of

(1E)-1-(4-fluorophenyl)-4-(4-pyridin-2ylpiperazin-1-yl)butan-1-one oxime;

(1Z)-1-(4-fluorophenyl)-4-(4-pyridin-2ylpiperazin-1-yl)butan-1-one oxime;

(1E)-1-(4-fluorophenyl)-4-(4-pyridin-2ylpiperazin-1-yl)butan-1-one methyloxime; and

(1E)-1-(4-fluorophenyl)-4-(4-pyridin-2ylpiperazin-1-yl)butan-1-one methyloxime.

45. (Cancelled) The method according to claim 40 wherein

```
X is O;
       R<sub>2</sub> is arylalkyl;
       and
       R<sub>4</sub> is heteroaryl.
46. (Cancelled) The method according to claim 40 wherein
       X is O;
       R<sub>2</sub> is arylalkyl wherein the arylalkyl is benzyl;
       R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-
2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.
47. (Cancelled) The method according to claim 40 wherein
        X is O;
        R<sub>2</sub> is heteroaryl;
        and
        R<sub>4</sub> is heteroaryl.
48. (Cancelled) The method according to claim 40 wherein
        X is O;
        R<sub>2</sub> is heteroaryl wherein the heteroaryl is pyridin-3-yl;
        and
        R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-
2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.
49. (Withdrawn)
                        The method according to claim 41 wherein
        X is O;
```

R₂ is aryl;

Z is C;

--- is a single bond; and R₄ is heteroaryl.

50. (Withdrawn) The method according to claim 41 wherein

X is O;

R₂ is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

Z is C;

--- is a single bond; and

R₄ is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

51. (Withdrawn) The method according to claim 41 wherein

X is O;

R₂ is aryl;

Z is CH;

--- is absent; and

R₄ is heteroaryl.

52. (Withdrawn) The method according to claim 41 wherein

X is O;

R₂ is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

Z is CH;

--- is absent; and

53. (Cancelled) The method according to claim 40 wherein

X is NRA;

R₂ is aryl;

and

R₄ is heteroaryl.

54. (Cancelled) The method according to claim 40 wherein

X is NR_A;

 R_2 is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

and

R₄ is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

55. (Withdrawn) The method according to claim 41 wherein

X is NR_A;

R₂ is aryl;

Z is CH;

--- is absent; and

R₄ is heteroaryl.

56. (Withdrawn) The method according to claim 41 wherein

X is NR_A;

 R_2 is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

Z is CH;

--- is absent; and

R₄ is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

57. (Withdrawn) The method according to claim 41 wherein R₃ is

58. (Withdrawn) The method according to claim 57 wherein

R2 is aryl; and

R₄ is heteroaryl.

59. (Withdrawn) The method according to claim 57 wherein

 R_2 is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

R₄ is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

60. (Withdrawn) The method according to claim 40 wherein R₃ is



61. (Withdrawn) The method according to claim 60 wherein

R₂ is aryl; and

R₄ is heteroaryl.

62. (Withdrawn) The method according to claim 60 wherein

R₂ is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

R₄ is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

63. (Cancelled) A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (Ia)

or a pharmaceutically acceptable salt thereof, wherein

X is selected from the group consisting of O and NR_A;

R_A is selected from the group consisting of hydrogen and alkyl;

R₁ is selected from the group consisting of hydrogen, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R₂ is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl; wherein the heteroaryl and the heteroaryl moiety of the heteroarylalkyl are mocyclic, five or six membered rings containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S;

R₃ is

R₄ is heteroaryl; wherein the heteroaryl is a monocyclic, five or six membered ring containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S;

L is alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl;

R_B is alkyl;

Z is N; and

--- is absent;

in combination with a pharmaceutically acceptable carrier.

- 64. (Cancelled) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or prodrug thereof in combination with a pharmaceutically acceptable carrier.
- 65. (Cancelled) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (Ia) according to claim 40 or a pharmaceutically acceptable salt thereof in combination with a phosphodiesterase 5 inhibitor.
- 66. (Cancelled) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (Ia) according to claim 40 or a pharmaceutically acceptable salt thereof in combination with an adrenergic receptor antagonist.
- 67. (Cancelled) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (Ia) according to claim 40 or a pharmaceutically acceptable salt thereof in combination with a dopamine agonist.
- 68. (Cancelled) A method of treating male erectile dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (Ia) according to claim 40 or a pharmaceutically acceptable salt thereof.

69. (Cancelled) A method of treating female sexual dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (Ia) according to claim 40 or a pharmaceutically acceptable salt thereof.

70. (Withdrawn) A method of treating cardiovascular disorders, attention deficit hyperactivity disorder, Alzheimer's disease, drug abuse, Parkinson's disease, schizophrenia, anxiety, mood disorders or depression in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (Ia) or a pharmaceutically acceptable salt or prodrug thereof.

71. (Withdrawn) A compound of formula (II)

$$R_1$$
 X
 N
 R_2
 II
 R_3

or a pharmaceutically acceptable salt or prodrug thereof, wherein

X is selected from the group consisting of O and NR_A;

R_A is selected from the group consisting of hydrogen and alkyl;

R₁ is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R₂ is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl;

R₃ is selected from the group consisting of

$$R_{4}$$
 R_{4}
 R_{4}
 R_{4}
 R_{4}
 R_{4}
 R_{4}
 R_{8}
 R_{8}
 R_{8}
 R_{8}

R₄ is aryl;

L is alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl; and

R_B is selected from the group consisting of hydrogen and alkyl.

72. (Withdrawn) The compound according to claim 70 wherein R_3 is

73. (Withdrawn) The compound according to claim 72 wherein

R₂ is aryl; and

R₄ is aryl.

74. (Withdrawn) The compound according to claim 72 wherein

 R_2 is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

 R_4 is aryl wherein the aryl is phenyl substituted with 0 or 1 substituent selected from the group consisting of alkoxy, cyano, and haloalkyl.

75. (Withdrawn) The compound according to claim 74 selected from the group consisting of

(1E)-1-(4-fluorophenyl)-3-{3-[3-(trifluoromethyl)phenyl]pyrrolidin-1-yl}propan-1-one O-methyloxime;

(1Z)-1-(4-fluorophenyl)-3-{3-[3-(trifluoromethyl)phenyl]pyrrolidin-1-yl}propan-1-one O-methyloxime;

1-(4-fluorophenyl)-3-[3-(2-methoxyphenyl)pyrrolidin-1-yl]propan-1-one Omethyloxime;

(1E)-1-(4-fluorophenyl)-3-[3-(3-methoxyphenyl)pyrrolidin-1-yl]propan-1-one Omethyloxime;

(1Z)-1-(4-fluorophenyl)-3-[3-(3-methoxyphenyl)pyrrolidin-1-yl]propan-1-one Omethyloxime;

(1E)-1-(4-fluorophenyl)-3-[3-(4-methoxyphenyl)pyrrolidin-1-yl]propan-1-one Omethyloxime; and

(1Z)-1-(4-fluorophenyl)-3-[3-(4-methoxyphenyl)pyrrolidin-1-yl]propan-1-one Omethyloxime.

76. (Withdrawn) The compound according to claim 70 wherein R₃ is

77. (Withdrawn) The compound according to claim 76 wherein

R₂ is aryl; and

R₄ is aryl.

78. (Withdrawn) The compound according to claim 76 wherein

R₂ is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

R₄ is aryl wherein the aryl is phenyl substituted with 0 or 1 substituent selected from the group consisting of alkoxy, cyano, and haloalkyl.

79. (Withdrawn) The compound according to claim 78 selected from the group consisting of

1-(4-fluorophenyl)-3-(3-phenylpiperidin-1-yl)propan-1-one O-methyloxime;

1-phenyl-3-(3-phenylpiperidin-1-yl)propan-1-one O-methyloxime; and

1-(4-chlorophenyl)-3-(3-phenylpiperidin-1-yl)propan-1-one O-methyloxime.

80. (Withdrawn) A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (II) in combination with a pharmaceutically acceptable carrier.

- 81. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with a pharmaceutically acceptable carrier.
- 82. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with a phosphodiesterase 5 inhibitor.
- 83. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with an adrenergic receptor antagonist.
- 84. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with a dopamine agonist.
- 85. (Withdrawn) A method of treating male erectile dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof.
- 86. (Withdrawn) A method of treating female sexual dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof.

87. (Withdrawn) A method of treating cardiovascular disorders, attention deficit hyperactivity disorder, Alzheimer's disease, drug abuse, Parkinson's disease, schizophrenia, anxiety, mood disorders or depression in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof.

88. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to said mammal in need of such treatment a therapeutically effective amount of a compound of formula (III)

$$\begin{array}{ccc}
R_1 \\
X \\
N \\
R_2
\end{array}$$
(III)

or a pharmaceutically acceptable salt or prodrug thereof, wherein

X is selected from the group consisting of O and NR_A;

R_A is selected from the group consisting of hydrogen and alkyl;

R₁ is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R₂ is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl;

R₃ is

R₄ is aryl;

L is alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl;

R_B is selected from the group consisting of hydrogen and alkyl;

Z is selected from the group consisting of C and CH; and

--- is absent or a single bond provided that when Z is C then --- is a single bond.

- 89. (Withdrawn) A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (III) in combination with a pharmaceutically acceptable carrier.
- 90. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with a pharmaceutically acceptable carrier.
- 91. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with a phosphodiesterase 5 inhibitor.
- 92. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with an adrenergic receptor antagonist.
- 93. (Withdrawn) A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with a dopamine agonist.
- 94. (Withdrawn) A method of treating male erectile dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof.
- 95. (Withdrawn) A method of treating female sexual dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically

effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof.

96. (Withdrawn) A method of treating cardiovascular disorders, inflammatory disorders, attention deficit hyperactivity disorder, Alzheimer's disease, drug abuse, Parkinson's disease, schizophrenia, anxiety, mood disorders or depression in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof.